[Cited Reference 7]

(TRANSLATION)
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Title of Invention: A tonic dichlorophenag (phonetic) sodium

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What Is Claimed:

[Claim 1] A tonic dichlorophenag (phonetic) sodium composition containing a rapidly releasing dichlorophenag sodium medical preparation and a gradually releasing dichoropheng sodium medical preparation, which is coated with the mixture of an intestine - soluble substance and a hydrophobic substance.

[Claim 2] A tonic dichlorophenag (phonetic) sodium composition as claimed in Claim 1, in which the intestine - soluble substance is one or more kinds of compounds selected from a hydroxy propyl methyl cellulose phthalate, a hydroxy propyl methyl cellulose acetate succinate, a cellulose acetate phthalate, a carboxy methyl ethyl cellulose and a methyl methacrylate · methahcrylic acid copolymer.

[Claim 3] A tonic dichlorophenag (phonetic) sodium composition as claimed in Claim 1, in which the hydrophobic substance is a water - insoluble high molecule.

[Claim 4] A tonic dichlorophenag (phonetic) sodium composition as claimed in Claim 1, in which the weight ratio of the rapidly releasing dichlorophenag sodium medical preparation to the gradually releasing dichorophenag sodium medical preparation as the dichlorophenag sodium is 1 : 9 to 4 : 6.

[Claim 5] A tonic dichlorophenag (phonetic) sodium composition as claimed in Claim 1 containing a plurality of gradually releasing dichlorophenag sodium medical preparations coated with another mixture in which the ratio of the intestine - soluble substance to the hydrophobic substance is different.

Detailed Explanation Of The Invention

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[The Means To Solve The Problems]

The present inventors have made extensive studies for long period of time

with the object of developing such a type of dichlorophenag (phonetic) sodium medical preparation in which the in - blood concentration of dichorophenag (phonetic) sodium can be maintained constant. As the result thereof, the present inventors have come to find that this object can be achieved by combining a rapidly releasing dichlorophenag sodium medical preparation with a gradually releasing dichorophenag sodium medical preparation coated with the mixture of an intestine - soluble substance and a hydrophobic substance, and further combining the same with a gradually releasing dichorophenag sodium in which the mixture amount of the intestine - soluble substance and the hydrophobic substance is different, thus completing the present invention.

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[0006]

[Form of Embodiments of the Invention] The dichlorophenag (phonetic) sodium medical preparation to be used in the present invention is in the form of an abstract or a granule agent which is obtained from dichlorophenag (phonetic) sodium and a well know medical additive according to the well known process for the preparation of a medical preparation. As the well known medical additive, it is possible to mention, for example, the shape - forming agents such as lactose, white sugar, D - mannitol, starches and so on; and bonding agents such as a hydroxy propyl cellulose, polyvinyl pyrroridone, gelatine and so on. By the way, if it is necessary, dichlorophenag sodium can be directly used as it is.

[0007] Further, the gradually released dichlorophenag sodium medical preparation to be used in the present invention is prepared by coating said abstract and granule with a mixture of an intestine - soluble substance and a hydrophobic substance.

[0008] As the intestine - soluble substance, it is possible to use a hydroxy propyl methyl cellulose phthalate (product name: HP), a hydroxy propyl methyl cellulose acetate succinate (product name: Shin-etsu AQOAT); a cellulose acetate terephthalate (product name: CAP), a carboxy methyl ethyl cellulose (product name: CMECAQ, OS); a methyl methacrylate · methacrylic acid copolymer (product name: Oidragid L and S); an ethyl methacrylate · methacrylic acid copolymer (product name: Oidragid L 30 D); and so on. It is also possible to use one or more kinds of these intestine - soluble substances. As these intestine - soluble substances, such a type kind is preferred that may have a solubility pH of 6.0 or greater.

[0009] As the hydrophobic substance, it is possible to mention hydrophobic high molecules such as an ethyl cellulose (product name: Ethocel), an ethyl cellulose water dispersion (Aquacoat), an aminoalkyl methacrylate copolymer (product name: Oidragid RS and NE 30 D) and so on. It is also possible to use one or more kinds of these hydrophobic substances.

[0010] The mixture ratio of said intestine - soluble substance to said hydrophobic substance is preferably in the range of 1 : 4 to 4 : 1 and further, normally a mixture of the intestine - soluble substance and the hydrophobic substance can be coated, on the basis of the rapidly released dichlorophenag sodium medical preparation, in

the range of 15 to 150 percent by weight.

[0015] Example 1:

1) Preparation of the rapidly released dichlorophenag sodium granule A:

1,410 g of purified white sugar spherical granule was put into a fluid layer coating apparatus, and 790 g of dichlorophenag sodium, 166 g of hydroxy propyl methyl cellulose; 34 g of talc; and 24 g of D - mannitol were suspended into 6,000 g of 10 - percent (w / w) ethanol. The thus obtained solution was spray - coated, according to the conventional method, onto the purified white sugar spherical granule and thereafter was dried at a temperature of 60 ℃ for one hour. The thus obtained product was used as the rapidly released dichlorophenag sodium granule A and the composition thereof is as follows;

dichlorophenag sodium	32.8 percent
hydroxy propyl methyl cellulose	6.3 percent
D - mannitol	0.9 percent
talc	1.3 percent
purified white sugar spherical granule	58.7 percent
Total:	100.0 percent

1) Preparation of the gradually released dichlorophenag sodium granule a:

800 g of gradually released dichlorophenag sodium was put into a fluid layer coating apparatus, and by the use of 4,000 g of the coating solution of the under - mentioned composition, the conventional coating was carried out thereby to obtain the gradually released dichlorophenag sodium granule a. The coated amount of this granule was about 50 percent on the basis of the rapidly released dichlorophenag sodium granule A.

Sin-etsu AQOAT AS - HF	4.5 percent
Ethocel	4.5 percent
Glycerine aliphatic acid ester	0.7 percent
Talc	0.7 percent
Ethanol	71.6 percent
Purified water	18.0 percent

Total: 100.0 percent

[0017] (3) Preparation of the tonic dichlorophenag sodium composition:

By charging a hard capsule with the rapidly released dichlorophenag sodium granule A and the gradually released dichlorophenag sodium granule a in the ratio of 3 : 7, such a type of capsuled agent was obtained that might contain 37.5 mg per capsule of dichlorophenag sodium.